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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/574,054 | 06/07/2006 | Youe-Kong Shue | 8031-011-US | 7988 |

32301 7590 04/07/2009

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| EXAMINER | |
|---|---|
| KRISHNAN, GANAPATHY | |
| ART UNIT | PAPER NUMBER |
| 1623 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 04/07/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/574,054 | SHUE ET AL. | |
| | Examiner | Art Unit | |
| | Ganapathy Krishnan | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

The amendment filed 12/22/2008 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 31-33 have been canceled.

2. Claims 1, 3, 6, 12, 19 and 22 have been amended.

3. Remarks drawn to rejections under 35 USC 112, first and second paragraphs, 102 and 103.

Claims 1-30 are pending in the case.

The following rejections have been overcome:

(a) The rejection of Claims 31-33 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of cartilage degradation, synovitis and subchondral bone edema, does not reasonably provide enablement for the prevention of the said conditions, has been rendered moot by cancellation of the said claims.

(b) The rejection of Claim 6 under 35 U.S.C. 112, second paragraph for reciting a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) has been overcome by amendment to claim 6. The rejection of Claims 31-33 under 35 U.S.C. 112, second paragraph for recitation of the relative term, 'less', has been rendered moot by cancellation of the claims 31-33.

(c) The rejection of Claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Henderson (US 5,587,363) has been overcome in view of applicants amendment to instant claim 1 and their arguments. Instant claim 1 now recites administration via intraarticular injection

(support in Specification at page 4 and page 18). Henderson teaches method of treatment wherein the aminosugar is administered orally as a capsule (col. 7, lines 65-67).

(d) The rejection of Claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Speck (US 4,870,061) has been overcome in view of applicants amendment to instant claim 1 and their arguments. Instant claim 1 now recites administration via intraarticular injection. Speck's teaching is mainly exemplified for buccal administration and to show that intramuscular injection of N-acetyl glucosamine introduces it into the joints. Intraarticular injection is not taught or exemplified.

The following rejection is made of record necessitated by amendment.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, 'wherein said treatment further comprises'. The said recitation means that the administration of the aminosugar is an additional step in the claimed method of treatment, which is performed after a treatment step that precedes it. The claim does not recite the step that precedes the administration of the aminosugar. This renders the claim indefinite. For the purpose of prosecution the claim is examined as drawn to treatment of the recited pathology comprising administration of the said aminosugar.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of Claims 18-19, 22-24 and 27-28 under 35 U.S.C. 102(b) as being anticipated by Henderson (US 5,587,363) is being maintained for reasons of record.

Applicants have traversed the rejection arguing that:

According to Henderson's disclosure only an aminosugar or only a glycosaminoglycan is insufficient for treating tissue damage. The compositions will not serve the purpose unless both components are included for conversion to proteoglycans for facilitating tissue repair. Henderson does not teach diagnosing a pathological marker as in instant claim 18 and injectable formulations as in instant claim 27. Applicants' arguments as they pertain to the current claims are not found to be persuasive.

Instant claim 18 is drawn to method treating joint condition comprising administration of an aminosugar. The term, administration is seen to include all forms of administration including the oral form as taught by Henderson. According to the instant specification (page 11, lines 5-11) cartilage degradation is a joint condition. Henderson teaches the use of compositions comprising glucosamine for the treatment of connective tissue and cartilage repair and arthritis/pain. The

aminosugar can be glucosamine or N-acetyl glucosamine or galactosamine or their salts (col. 3, line 34 through col. 4, lines 16-63; col. 6, lines 49-56; col. 8, Case #1; col. 6, lines 48-56; col. 7, lines 57-61). Repair is done by manufacture of collagen, which needs proteoglycans and for the production of proteoglycans glucosamine is needed (col. 1, line 54 through col. 2, line 51). Glucosamine is also known to localize in cartilage and joint tissues (col. 4, lines 47-52). Henderson also teaches dosages of the aminosugars for the said treatments (col. 8, lines 1-49; col. 11 line 15 through col. 12, line 46). According to Henderson's teaching (col. 2, line 37 to col. 3, line 31, as pointed out by applicants) the individual use of GAG's and glucosamine have been useful for intended purpose including degenerative joint afflictions (col. 2, lines 55-59). This means that aminosugars alone are useful for treatment of joint afflictions like cartilage degradation even though they may have varying degrees of effectiveness. Instant claim 18 recites the term comprising, which is open ended language. Hence, the teaching of Henderson is seen to anticipate the instant claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 1-30 under 35 U.S.C. 103(a) as being unpatentable Henderson (US 5,587,363) in view of Speck (US 4,870,061), Nanba et al (US 5,169,636), Burger (US

5,843,919), Woerly (US 5,863,551), Evans et al (US 6,506,785) and Wong et al (WO 00/68194) is being maintained for reasons of record.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Henderson teaches the use of compositions comprising glucosamine for the treatment of connective tissue and cartilage repair and arthritis/pain. The aminosugar can be glucosamine or N-acetyl glucosamine or galactosamine or their salts (col. 3, line 34 through col. 4, lines 16-63; col. 6, lines 49-56; col. 8, Case #1; col. 6, lines 48-56; col. 7, lines 57-61). According to Henderson, connective tissues of humans and animals are constantly subjected to stresses and strains that can result in afflictions such as arthritis, joint inflammation (sports related injury; col. 1, lines 23-31). Repair is done by manufacture of collagen, which needs proteoglycans and for

the production of proteoglycans glucosamine is needed (col. 1, line54 through col. 2, line 51). Glucosamine is also known to localize in cartilage and joint tissues (col. 4, lines 47-52). Henderson also teaches dosages of the aminosugars for the said treatments (col. 8, lines 1-49; col. 11 line 15 through col. 12, line 46).

Speck, drawn to a method of treating degenerative joint disease (joint cartilage), suggests the use of N-acetyl glucosamine in combination with excipients via intraarticular, intramuscular, intravenous, or other injection or infusion methods (col. 1, lines 1-67; col. 3, lines 58-61; col. 5 line 15 through col. 6, line 34). Even though Speck does not exemplify the treatment of joint diseases via intraarticular injection of the aminosugar he suggests such a method of administration. According to Speck, glucosamine administered via injection is effective (col. 2, lines 16-18).

However, Henderson and Speck do not exemplify the use of aminosugars in the treatment of synovitis and subchondral bone edema and also the use of various forms of the composition comprising them like liposome, nanosphere suspension, implant gel, controlled release, etc and also the use of the aminosugars of their invention in combination with anti-inflammatory drugs and hexoaminidase inhibitors.

Nanba et al, drawn to liposomes, teach compositions comprising oligosaccharides comprising glucosamine and galactosamine residues entrapped by liposomes (col. 1, lines 60 col. 2, line 68). Phospholipids like distearoylphosphatidylcholine are suggested for use in the liposome preparations. Charged lipids like phosphatidylserine are suggested for use inorder to prevent leakage of the entrapped agents (col. 4, lines 8-27). The liposomes containing the aminosugars are made into particles having a diameter of about 0.03-0.8 microns (microspheres,

col. 5, lines 43-46). According to Nanba liposomes are models for biological membranes and are effective in stabilizing drugs and achieving sustained release of drugs in vivo. The duration of the efficacy of drugs can be prolonged (col. 1, lines 25-28; lines 37-39). Even though Nanba teaches oligosaccharides comprising glucosamine and galactosamine residues, one of skill in the art will recognize that the monomeric aminosugars can also be use to make the same liposomal formulations.

Burger, drawn to arthritis/osteoarthritis, teaches the treatment of these conditions using compositions of comprising a combination glucosamine and N-acetyl glucosamine (col. 2, lines 19-44). The said compositions are preferably in the form of solutions, suspensions, gels, systemic implant or an injection or injection into an affected joint (col. 3, lines 20-56).

Woerly teaches polymer hydrogels as implants for treating tissue replacement and regeneration (col. 1, lines 5-18). Another aspect of his invention is the use of a polymer matrix (col. 5, lines 33-40 and lines 52-56). The polymer matrices can include aminosugars like glucosamine, N-acetyl glucosamine, galactosamine and N-acetylgalactosamine (col. 8, lines 31-34). Even though Woerly does not exemplify the use of such matrices for the treatment of specific conditions as instantly claimed one of skill in the art will recognize that such matrices containing the monomeric aminosugars can be made and used for the treatment of degenerative diseases and conditions as instantly claimed.

Evans, drawn to cartilage degradation and subchondral bone, teaches a method of treating the same using antiinflammatory agents in combination with glucosamine in different forms and modes of administration for the treatment of articular cartilage degeneration including timed release and controlled release or a depot (abstract; col. 7, lines 49; col. 8, lines 3-31; col. 9, line

26 through col. 10, line 25). Even though Evans teaches the use of glucosamine and antiinflammatory agent sin combination with the compound of formula (I) of his invention, one of skill in the art will recognize that glucosamine and the antiinflammtory agents alone could be used in the said forms and modes of delivery for the said treatment since the use of glucosamine alone for the treatment of cartilage degradation is taught in the prior art. The Examiner would like to point out that even though Evans teaches method of prevention of the said conditions Example 1 (col. 36; lines 39-46) teaches that osteoarthritis was induced in animals before administration of the active agents. This is seen as a method of treatment and not prevention.

Wong et al teach that hexoaminidases catalyze the myriad of processes, one of which is cartilage erosion in arthritic subjects from over catabolism of glycosaminoglycans that fill the cartilage tissue. Wong specifically teaches development of iminocyclitols as inhibitors of hexoaminidases (page 1, line 5 through page 2, line 13; page 2, lines 33-39). This means that iminocyclitols can be used in combination with glucosamine and galactosamine and their salts and their N-acyl derivatives for the treatment of cartilage degradation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as instantly claimed since the active agents and the methods of treatment using them individually are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions and modes of administration and use them in a method of treatment of cartilage degradation, synovitis and subchondral bone edema as instantly claimed since the use of active agents like glucosamine, galactosamine and

iminocyclitols since aminosugars like glucosamine are responsible for the synthesis of proteoglycans needed for cartilage/tissue repair and the said aminosugars are well known agents for the said treatment as taught in the prior art above. Also, according to Henderson and Speck, administration of glucosamine via injection is known to concentrate in the joints.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms since similarity in structure and function/utility entail motivation for use in the instant compositions and methods. One of skill in the art would also be motivated to look for other active agents and formulation that are more efficient and have enhanced beneficial effects.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980.

## *Conclusion*

Claims 1-30 are rejected

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623